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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,266	02/26/2004	Thomas Jessel	5199-169	9559

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EXAMINER	
GAMETT, DANIEL C	

ART UNIT	PAPER NUMBER
1647	

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04/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/789,266	JESSEL ET AL.	
	Examiner	Art Unit	
	Daniel C. Gamett, PhD	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-67* is/are pending in the application.

4a) Of the above claim(s) *1-42 and 53-67* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *01/18/2005 12/13/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of claims 43-52 in the reply filed on 02/14/2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Applicant's election of FGF as the species of modulator of the FGF signaling pathway in the reply filed on 02/14/2007 is acknowledged. Applicant expressed some confusion as to the requirement for election of species. Applicant's assumption that the intent was to identify claim 49, and select from activators of an FGF signaling pathway is correct, especially in view of section 7 of the requirement for election/restriction mailed on 08/14/2006. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 1-42 and 53-67 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 02/14/2007.

4. Claims 43-52 are under consideration insofar as the read upon methods wherein the activator of an FGF signaling pathway is an FGF protein.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 43-52 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for identifying a modulator of an FGF signaling pathway wherein the activator of an FGF signaling pathway is an FGF protein, does not reasonably provide enablement for methods wherein the activator of an FGF signaling pathway is anything other that an FGF protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Claims 43-49, 51 and 52 are drawn to methods for identifying a modulator of an FGF signaling pathway. The methods comprise incubating cells with an "activator of an FGF signaling pathway". The specification provides at [0176-0177] a broad definition and non-limiting exemplary list for the term "activator of an FGF signaling pathway". The list appropriately includes each of the known FGF proteins. The also list includes molecules which are not known to be directly involved with FGF signaling and for which any association with FGF signaling stems from common usage of intracellular pathways (e.g. ras, PKC, PI3K) shared by many growth factors. The list therefore includes signaling molecules that are not specific to FGF signaling, some of which are identified in the specification. VEGF, for example, is identified as an activator of both Wnt and FGF signaling [0143, 0177]. TGFβ is identified as an activator of BMP, Hh, and FGF signaling [0154, 0163, 0177]. The specification provides no guidance as one could identify a modulator of an FGF signaling pathway if any of these molecules were used as the "activator of FGF signaling" in the claimed method. If, for example, VEGF were the "activator of FGF signaling", a test compound that gave a measurable result would identified as a modulator of VEGF signaling, but the result would not show that the test

compound acts on a component of VEGF signaling shared with FGF. Further experimentation would be required to determine if the test compound actually modulates an FGF signaling pathway. The same can be said of any of the named growth factors and cytokines in [0177] and claim 49. The claimed method cannot identify a modulator of an FGF signaling pathway unless a known activator of an FGF signaling pathway is used. By encouraging the skilled artisan to employ molecules that are only coincidently related to FGF signaling, the specification actually guides the skilled artisan away from identifying a modulator of an FGF signaling pathway.

7. Claim 50 is directed to a method of identifying a modulator of neural differentiation. The recited steps could achieve this goal because they do provide for a determination of neural differentiation. However, this claim, along with claims 43-49, 51 and 52, still directs the artisan to contact cells with any one of a plethora of "activators'. Many of the "activators" are intracellular molecules, such as ras, raf Grb2, PI3 kinase, MEK, PIP2, PKC, PLC, PTN, and etc. The specification does not provide for cells that do not intrinsically possess these molecules and so does not teach the skilled artisan how to controllably contact cells with these "activators". In addition to the multitude of named "activators", the list also includes "any analogue or homologue thereof". The skilled artisan would be required to perform undue experimentation order to practice any of the methods of claims 43-52 with this indeterminably large genus of reagents.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 43, 46, and 48-52 are rejected under 35 U.S.C. 102(b) as being anticipated by Ghosh *et al.*, Neuron, 15: 89-03, 1995. Independent claims 43 and 50 are drawn to nearly identical methods in which two matched collections of cells are contacted with a candidate modulator in the presence of an activator of an FGF signaling pathway or with an activator of an FGF signaling pathway alone, and neural differentiation in the two cell collections is compared. Claim 51 is drawn to apparently the same method for determining if the candidate modulator modulates FGF-dependent neural differentiation; claim 52 recites contacting cells with the candidate modulator in the presence of an activator of an FGF signaling pathway. In the experiment shown in figure 9 in Ghosh *et al.*, neural progenitor cells were incubated in the presence of bFGF with or without the additional presence of either NT-3 (panel D) or anti-NT3 antibody (panel B). This experiment, therefore, teaches the instantly claimed methods, with NT-3

and anti-NT3 antibody as candidate modulators. NT-3 was observed to enhance neural differentiation (see panel D), thereby anticipating instant claim 48.

10. Claims 43-46 and 48-52 are rejected under 35 U.S.C. 102(b) as being anticipated by Lee *et al.*, Nature Biotech. 18:675-678 (2000) (of record, IDS 01/18/2005). Lee *et al.* teach the generation of neurons from embryonic stem cells. In the experiment shown in figure 5 of Lee *et al.*, embryonic stem cells (including neural progenitors derived from embryonic stem cells) were incubated in the presence of FGF with or without the additional presence of SHH. This experiment, therefore, teaches the instantly claimed methods, with SHH as a candidate modulator. SHH was observed to enhance neural differentiation (see panel B), thereby anticipating instant claim 48.

11. Claims 43-52 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent Application publication 20040092012 (Okano), filed October 3, 2001. Okano teaches methods for producing motor neurons from embryonic stem cells within embryoid bodies; the method employs a medium containing a fibroblast growth factor (FGF) and a sonic hedgehog protein [0004, 0019, 0020]. In the experiment shown in figures 7 and 8 of Okano, embryonic stem cells (including neural progenitors derived from embryonic stem cells) were incubated in the presence of FGF with or without the additional presence of noggin or SHH. These experiments, therefore, teach the instantly claimed methods, with noggin and SHH as candidate modulators, each of which were observed to enhance differentiation of motor neurons.

Conclusion

12. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel C Gamett, Ph.D., whose telephone number is 571 272 1853. The examiner can normally be reached on M-F, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571 272 0961. The fax phone number for the organization where this application or proceeding is assigned is 571 273 8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

DCG
Art Unit 1647
20 April 2007

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